Clinical Evaluation of i-STAT 500® Analyzer for Glucose, Hematocrit and Sodium

Abbott Point of Care (APOC)

WARNING:

FOR INVESTIGATIONAL USE ONLY. The performance characteristics of this product have not been established. No clinical decision or patient notification should be made based on the results obtained with this product.

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Rationale for amendment: Incorporates Scientific Changes

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Revision Number	Effective Date	Reason for revision
02	21-March-2016	Initial Release
03	05-May-2016	Heparinized capillary tubes are required for the study. Revisions were made on pages 7, 12 and 13 to include "balanced heparin capillary tubes".
04	30-Jun-2016	Added sentence to reference that the i-STAT EC4+ cartridge also tests for potassium and hemoglobin. The results for potassium and hemoglobin will be collected for informational purposes only (page 6). Reference to potassium and hemoglobin results will be collected but used for informational purposes only and entered into the electronic case report forms by site personnel (page 15).
05	22-Jul-2016	Clarified collection and test times for native and contrived whole blood samples.
06	04-Oct-2016	Change 1 **Change**: The number of specimens to be collected per site has been increased from approximately 40-55 to approximately 100. **Reason:** To allow for collecting an increased number of samples and samples sourced by the clinical sites. **Justification:** To provide sufficient number of specimens to cover the range of concentrations required for the three study analytes. Change 2 **Change**: Extended the duration of the study from 10 weeks to 16 weeks. **Reason**: To ensure all samples needed per the study protocol are obtained and received and tested by the clinical sites. **Justification**: To allow for completion of all study related activities within the given timeframe of the study protocol.

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I. Introduction

The i-STAT® System is an *in vitro* diagnostic test system which uses a portable clinical analyzer and single-use cartridge to perform simultaneous quantitative determination of specific analytes in whole blood.

The i-STAT 500 analyzer is intended to be used by trained medical professionals for a variety of in vitro diagnostic tests and test panels using i-STAT test cartridges.

The i-STAT 500 is an updated version of the i-STAT 1 Wireless clinical analyzer. The Abbott monitor will provide the i-STAT 500 Quick Reference Guide, which contains the instructions for use of the new i-STAT 500 analyzer.

The performance of the investigational i-STAT 500 analyzer will be evaluated based on results of method comparison testing, as described in this protocol. Tests for glucose, hematocrit and sodium will be used to perform the evaluation for capillary specimens.

The test for glucose, as part of the i-STAT System, is intended for use in the *in vitro* quantification of glucose in arterial, venous, or capillary whole blood. Glucose measurements are used in the diagnosis, monitoring, and treatment of carbohydrate metabolism disorders including, but not limited to, diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma. This protocol will focus on glucose testing for capillary specimens only.

The test for hematocrit, as part of the i-STAT System, is intended for use in the *in vitro* quantification of packed red blood cell volume fraction in arterial, venous, or capillary whole blood. Hematocrit measurements can aid in the determination and monitoring of normal or abnormal total red cell volume status including, but not limited to, conditions such as anemia, erythrocytosis, and blood loss related to trauma and surgery. The i-STAT System provides a calculated hemoglobin result using the hematocrit result. This protocol will focus on hematocrit testing for capillary specimens only.

The tests for sodium, as part of the i-STAT System, are intended for use in the *in vitro* quantitation of sodium in arterial, venous or capillary whole blood. Sodium measurements are used for monitoring electrolyte imbalances. This protocol will focus on sodium testing for capillary specimens only.

This study will be conducted in compliance with this protocol, Good Clinical Practice (GCP) and the applicable regulatory requirements.

II. Objectives

The objective of this study is to compare the performance of the i-STAT 500 analyzer to the marketed i-STAT 1 Wireless analyzer in a Point-of-Care (POC)

setting. The evaluation will be performed using the i-STAT EC4+ cartridge to test glucose, hematocrit and sodium on capillary specimens.

The i-STAT EC4+ cartridge also tests for potassium and hemoglobin. The results for potassium and hemoglobin will be collected for informational purposes only.

III. Study Design

A. Overview

Protocol directed testing will be performed at a minimum of three (3) external US sites to evaluate the i-STAT 500 analyzer for performance compared to the marketed i-STAT 1 Wireless analyzer using clinical specimens. For this study, the i-STAT EC4+ cartridge will be used to evaluate the results reported for glucose, hematocrit, and sodium.

Method Comparison

Method comparison testing will be performed using prospectively collected native capillary specimens. This testing will be performed at a minimum of three (3) sites. Testing of approximately 120 native specimens will be performed in singlicate on both the i-STAT 500 analyzer and the i-STAT 1 Wireless analyzer. One (1) i-STAT 500 analyzer and one (1) i-STAT 1 Wireless analyzer will be used for this testing. Sufficient subjects must be enrolled to meet a minimum of 120 eligible subjects for study analysis. Each site will collect and test approximately 100 specimens until sufficient capillary specimens are collected and tested for study analysis. A minimum of one (1) lot of i-STAT EC4+ cartridges will be used for this testing.

Sufficient specimens for each analyte within their respective target ranges must be obtained to meet the minimum requirement of eligible specimens for study analysis. Requirements for the study are:

Analyte	Capillary
Glucose	120
Hematocrit	120
Sodium	120

B. Ethics

Capillary specimens for use in this study will be prospectively collected with informed consent. Study subjects (or legally authorized representatives, if applicable) must confirm their willingness to participate in the study by signing and dating an Institutional Review Board (IRB) approved consent form prior to the collection of the specimens or other study-related information.

The investigator will ensure that an IRB has approved the protocol and written informed consent (if needed) prior to subject participation in this clinical study. The approval letter must be signed by the IRB chairman or authorized representative prior to the start of this clinical study.

Until the clinical study is completed, the Investigator will advise their IRB of the progress of this clinical study, per IRB requirements. Written approval must be obtained from the IRB annually (or more frequently if required by the IRB) to continue the clinical study, according to each institution's IRB requirements. Further, any amendments to the protocol as well as associated informed consent form changes will be submitted to the IRB and written approval obtained prior to implementation, according to each institution's IRB requirements.

All reports transferred to and communications with Abbott which pertain to specimens in the study must identify each specimen by a study number to ensure subject confidentiality.

C. General Schedule of Events

Study testing personnel will be required to demonstrate acceptable performance with the i-STAT 1 Wireless analyzer and the i-STAT 500 prior to beginning study-directed procedures. The Abbott monitor will observe testing of training material and confirm that the correct procedural steps were taken and that acceptable results were obtained.

After successful completion of the training, testing personnel will complete the study-directed procedures as described in this protocol.

Specimens will be identified using a study identification number (SID).

Case Report Forms (CRF) will be utilized to document completion of the test procedures. The Abbott monitor will review the data and CRF to assure compliance to the study-directed procedures and to monitor the progress of the study.

The study will take approximately 16 weeks to complete depending on the ability of the site to source specimens.

D. Comparator Method

For method comparison, the comparator testing will be performed using the i-STAT

1 Wireless analyzer. All specimens will be tested using the FDA cleared i-STAT EC4+ cartridge. Comparator testing will be performed at a minimum of 3 sites. Testing will be performed as instructed in the i-STAT 1 System Manual and instructions for use of the test cartridge. The i-STAT 1 Wireless analyzer and peripherals will be supplied by Abbott.

The glucose, hematocrit and sodium results from the i-STAT 1 Wireless will be compared to the corresponding glucose, hematocrit and sodium results of the i-STAT 500.

IV. Operating Conditions

A. Material and Equipment

1. Product Description

Products, supplies, and materials listed below will be supplied by Abbott Laboratories.

The investigational products for use in this study are as follows**:**

- i-STAT 500 analyzer, List No. 023065-01
- Specific hardware for use with investigational product:
  - i-STAT 500 Rechargeable Battery, List No. 027642-01
  - i-STAT 500 Base Station, List No. 026159-01
  - i-STAT 500 Electronic Simulator, List No. 040018-01
  - i-STAT 500 Printer Kit, List No. 025913-01

The marketed products for use in this study are as follows**:**

- i-STAT 1 Wireless analyzer, List No. 03P75-01
- Electronic simulator, List No. 06F11-01
- i-STAT EC4+ cartridges, List No. 03P81-25
- i-STAT TriControls
  - Level 1, List No. 05P71-01
  - Level 2, List No. 05P72-01
  - Level 3, List No. 05P73-01
- i-STAT Printer, List No. 04P74-04
- i-STAT Printer paper
- Lithium Batteries for the i-STAT 1 analyzer, List No.06F21-26

Additional materials to be supplied by Abbott:

- Capillary Tubes, Plain
- Capillary Tubes, Balanced Heparin (150µL)
- BD Microtainer Contact Activated Lancets, PN 366594 (Blade 1.5mm wide x 2.0mm deep)

- PDI Super Sani-Cloth Germicidal Disposable Wipes
- CaviWipes Disinfecting Towelettes

Materials to be supplied by the site:

- Gauze
- Sharps Container

Expired material(s) must not be used.

A description of the investigational product is presented in the i-STAT 500 Quick Reference Guide.

2. Product Storage and Handling Requirements

The i-STAT 500 analyzer and any other study materials and equipment provided by Abbott should be segregated and stored in a secured location.

All commercially available products will be handled according to the manufacturer's package insert instructions and product labeling.

Secured storage of these supplies with appropriately restricted access is required.

3. Instructions for Use

Testing on the i-STAT 500 for this study will follow the procedures in this clinical protocol and the i-STAT 500 Quick Reference Guide in conjunction with the i-STAT 1 System Manual for information that is common to both the i-STAT 1 Wireless and the i-STAT 500 analyzers.

All versions of the i-STAT 500 Quick Reference Guide will be retained in the Abbott clinical study files. For this study, relevant sections of the i-STAT 1 System Manual will be provided by the Abbott Monitor.

B. Environment

Testing personnel for this study will include testers that are representative of Point of Care End Users such as point of care coordinators, nurses, respiratory therapists, medical assistants or physicians.

C. Personnel Requirements

The investigator and all study staff will be trained on the clinical protocol.
The investigator and all study staff involved in the prospective collection of specimens must have completed Collaborative IRB Training Initiative (CITI) in the protection of human research subjects and Good Clinical Practice training, or equivalent.

Personnel involved in execution of the i-STAT analyzer testing must be trained on or have documented experience operating and maintaining the i-STAT 500 analyzer and the i-STAT 1 Wireless analyzer. Each individual will also be trained on the i-STAT 500 Quick Reference Guide and will be required to demonstrate their ability to use the investigational analyzer prior to beginning the Testing Procedures described in this protocol.

V. Product Accountability

The clinical testing sites must maintain records and accountability documentation of the receipt dates, lot numbers, quantities, and the use, destruction and/or return of all investigational products. The Abbott monitor will periodically verify the accuracy of these inventories.
All investigational products must be returned to Abbott or disposed of on-site. An investigator will not supply investigational products to any individual who is not named as a study investigator.

VI. Study Methods and Procedures

A. Specimen Handling and Accountability

Specimens must be processed according to the requirements defined in this protocol and instructions provided by the Abbott monitor. Refer to the i-STAT 1 Manual for instructions on the procedures for collection and testing of capillary whole blood specimens.

A specimen may be withdrawn from the study if the sample is found unacceptable for testing (e.g. inappropriate handling prior to testing, inadequate volume), or for other assignable causes. The reason for removal must be documented. The Abbott monitor must be notified if a specimen is being considered for withdrawal. Specimens withdrawn from the study may need to be replaced, if deemed necessary by the Abbott monitor, to meet requirements for the minimum number of specimens.

B. General Study Procedures

1. General Procedures for Use of the i-STAT 500 Analyzer

- Refer to the i-STAT 500 Quick Reference Guide for instructions on the use of the analyzer.
- Refer to the i-STAT 500 Quick Reference Guide for instructions on cleaning and disinfecting the analyzer.

- An Electronic Simulator test should be completed for each i-STAT 500 analyzer received. This should be performed prior to study directed testing. The successful completion of the Electronic Simulator check must be documented in the CRF.

- If a test result is flagged (i.e. *** or < >) or a quality check code is displayed during study-directed testing, the data tape should be printed for all tests and the data entered into the appropriate eCRF. For quality check codes, complete an Incident CRF and document the action taken.

2. Calibration

Calibration curves are standardized during manufacturing and adjustments, if required, are made during regular software updates. No operator intervention is needed.

3. Operator Proficiency

Training materials (e.g., training panel and/or test controls) will be used to assess investigational analyzer proficiency. Analyzer proficiency with both i-STAT 500 and i-STAT 1 Wireless is to be performed by each user. Proficiency testing details will be provided by Abbott. The Abbott monitor will evaluate the results for acceptability. The results of the proficiency testing will be documented in the study files.

4. Cartridge Quality Control

A temperature monitoring check must be performed for acceptance of the received cartridges. Check the temperature indicator strip included in the shipping container. If the 3rd and 4th windows on the strip are colored, the cartridges should not be used and the Abbott monitor should be contacted. Complete the shipping and receipt information on the strip card.

The i-STAT TriControls Level 1, 2 and 3 are to be tested on the i-STAT 1 Wireless for each new shipment of cartridges received. The results obtained should be within the expected values in the Value Assignment Sheet. If a quality check code is generated or any result is out of range, repeat the control testing with a fresh ampule. If a second quality check code is generated or the result is still outside the expected range, contact the Abbott monitor. An incident CRF should be completed, documenting the action taken. Data tapes for all tests should be printed and entered into the appropriate eCRF.

C. Testing Procedures

1. Method Comparison for Capillary Specimens

a) Specimen Selection

i) Study Population/Sample Size

The site will source capillary specimens by prospective collection with informed consent.

For glucose a minimum of 120 capillary specimens that span the measuring interval of glucose will be tested. Each site will source approximately 100 specimens until sufficient capillary specimens are collected and tested.

For hematocrit a minimum of 120 capillary specimens that span the measuring interval of hematocrit will be tested. Each site will source approximately 100 specimens until sufficient capillary specimens are collected and tested.

For sodium a minimum of 120 capillary specimens that span the measuring interval of sodium will be tested. Each site will source approximately 100 specimens until sufficient capillary specimens are collected and tested.

Sites should attempt to source capillary specimens from all target levels. If all target levels cannot be sourced from native specimens, specimens may be contrived. An Abbott representative will assist with contriving specimens in accordance to an Abbott representative procedure that will be included in the study files.

Should a contrived sample not meet the expected target concentration after contriving, the subject may be withdrawn from the study, ensuring to document the reason for withdrawal.

A suggested distribution of capillary specimen target levels for glucose, hematocrit and sodium by site is presented in the chart below.

Glucose (mg/dL)	~ # Sample/Site
≤ 50	2
> 50-80	4
> 80-120	8
> 120-200	12
> 200-300	6
> 300-400	4
> 400-500	2
>500	2
Total	**40**

Hct (%PCV)	~ # Sample/Site
<27	6
27 – 35	10
36 – 50	20
>50	4
Total	**40**

Na (mmol/L)	~ # Sample/Site
≤ 130	8
131-140	16
141-150	12
>150	4
Total	**40**

ii) Subject Inclusion and Exclusion Criteria

Prospectively collected specimens should be from unique individuals.

Inclusion Criteria

- Subject is ≥ 18 years of age
- Subjects (or their legal representative) who are willing to voluntarily consent to the study

Exclusion Criteria

- There are no exclusion criteria

iii) Specimen Collection

To obtain native capillary specimens, skin punctures will be performed on two fingers. The first skin puncture will be used to fill a balanced heparin capillary tube and transfer the sample to the i-STAT 1 Wireless analyzer. The second skin puncture will be used to fill a balanced heparin capillary tube and transfer the sample to the i-STAT 500 analyzer.

A minimum of 150 µL of whole blood per individual capillary tube specimen is required to complete testing.

If insufficient volume of whole blood is obtained in order to test on both the i-STAT 1 Wireless and i-STAT 500 analyzer, the subject may be asked to return for a repeat collection. To be eligible for participation in this study the same subject must have signed and dated an informed

consent form for allowance of up to 4 skin punctures, prior to prospective collection of a whole blood specimen.

For specimens that will be contrived, a maximum of 3 mL of venous blood specimen and/or a minimum of 250 µL capillary blood is required to complete method comparison testing.

Each specimen will be given a unique study identification number (SID). The date and time of collection, the specimen type (native or contrived), and collection device (capillary), as applicable will be documented.

b) Procedure

Capillary specimen method comparison will be performed at a minimum of 3 sites. Specimens will be tested on one (1) i-STAT 500 analyzer and one (1) i-STAT 1 Wireless analyzer. A minimum of one lot of i-STAT EC4+ cartridges per site will be used for this testing.

Per the i-STAT 500 Quick Reference Guide, the Study Workflow and the i-STAT 1 System Manual, collect specimen and perform testing in the Patient pathway on the i-STAT 500 menu.

1. Ensure at least two (2) i-STAT EC4+ cartridges are at room temperature.
2. Prepare one i-STAT 500 analyzer and one i-STAT 1 Wireless Analyzer.
3. Collect specimen. If required, contrive the specimen per Abbott Instructions.

Note: Testing for native or contrived whole blood specimens collected in balanced heparin capillary tubes must be within 3 minutes of collection. Test time is defined as the difference between sample collection time and the time when the cartridge is inserted into the device. Collection time is defined as the time when a sufficient volume of capillary sample is obtained.

Note: A separate capillary tube must be used for each cartridge fill.

4. Fill and Test Cartridges:

a) Place the first cartridge on a flat surface or hold it in a horizontal position.

b) Direct the tip of the capillary into the sample well.

c) Dispense sample slowly and steadily until it reaches the fill mark indicated on the cartridge label. Leave some sample in the sample well.

d) Fold the snap closure over the sample well.

e) Press the rounded end of the closure until it snaps into place. Slightly lift finger or thumb and ensure that the cartridge is closed before completely removing finger or thumb from the closure.

f) Insert the cartridges into the i-STAT 1 Wireless analyzer before proceeding to the next cartridge.

g) Using a new capillary tube, repeat steps 3- 4 and 4a-4e for the second i-STAT EC4+ cartridge (using a capillary specimen from the second fingerstick). Place the cartridge into the i-STAT 500 analyzer.

After the results are displayed, remove and discard the cartridges.

Print the results and tape them to the appropriate study form.

If a test result is flagged with *** or a quality check code is displayed, a repeat of the testing procedure on both the i-STAT 1 Wireless and the i-STAT 500 analyzer may be performed with new cartridges from the same subject. The subject must be eligible for repeat participation as per agreement in the signed and dated an informed consent form prior to prospective collection of a whole blood specimen. If the result is suppressed again, contact the Abbott monitor. The code that identifies the problem should be recorded on the Incident CRF.

VII. Methods for Data Collection and Documentation

A. Data Collection

All results (numerical or flagged) will be printed from the i-STAT 500 and the i-STAT 1 Wireless analyzer to a portable printer. Refer to the i-STAT 500 Quick Reference Guide and the i-STAT 1 System Manual for printing instructions. Results will be printed on thermal paper and labeled for Investigational Use Only. Data printed on thermal paper must be photocopied or captured via electronic storage media (e.g. electronic systems such as tablets). If photocopied, the original and photocopy of the analyzer printouts are to remain with the site's study files. A second copy of the printouts should be made and to be sent to the Abbott monitor as they are completed. If captured via electronic storage, the original data tape may be either be stored in the site's study file or sent to the Abbott monitor.

All i-STAT results will be entered into electronic case report forms by site personnel. If any i-STAT results cannot be entered into the case report form, the data will be manually entered into the database at Abbott using the analyzer printout.

Potassium and hemoglobin results will be collected and entered into the electronic case report forms by site personnel. These results will be used by Abbott for informational purposes only.

B. Case Report Forms

CRF for collection of data will be supplied by Abbott including detailed instructions for completion of these forms.

CRF data or information related to the study will be recorded electronically using a web based system. Photo images of source data will be attached to the electronic CRF. Site personnel responsible for entering data will be trained on the use of the electronic system (i.e., access, entry and submission of data, photo file attachments). Data entered by the site will be reviewed by an Abbott monitor, and queried if needed. Queries should be resolved in a timely manner.

Data or information recorded on the CRF with no prior written or electronic record, (e.g., specimen processing, storage date and time) will be considered the source document.

The investigator must sign the CRF where indicated. The investigator's signature indicates that the data are accurate and complete. Where signatures are required they must be handwritten or captured electronically per 21 CFR Part 11. Stamps for signatures are not allowed.

At the conclusion of the study, a copy of the completed CRF will be maintained at each investigational site and a backup copy stored at Abbott.

VIII. Adverse Events

A **Subject Adverse Event** is any unfavorable or unintended medical occurrence (e.g., sign, symptom, or disease) temporally associated with the specimen collection procedure performed.

A **Subject Serious Adverse Event** is an untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity, or
- results in a congenital anomaly/birth defect.

A **Device Adverse Event** is any effect on the health or safety of an individual associated with the use of a product that has or may have caused or contributed to an injury, a system malfunction or user error resulting in personal injury (e.g., electrical shocks, burns, etc.), or exposure to potentially hazardous material (e.g., chemical or biohazardous), or a fire or visible smoke that was not self-contained to the system and caused damage outside of the system.

A **Device Serious Adverse Event** is an adverse event that has or may have caused or contributed to a death or serious injury of an individual or an adverse event resulting from malfunction that could cause or contribute to a death or serious injury if the malfunction were to recur. A serious injury includes a life-threatening illness or injury, an illness or injury, which results in permanent impairment of a body function or permanent, irreversible damage to body structure, or a condition, an injury or illness necessitating a medical or surgical intervention by a health care professional to prevent permanent, irreversible impairment of a body function, or damage to a body structure.

It is expected that drawing blood may cause pain, bruising, lightheadedness, and on rare occasion, infection at the site of the blood draw. These events will not be recorded as adverse events as they are considered to be normal events that may occur during the course of a blood draw. Other events that may occur such as fainting, that are not routinely associated with a blood draw, must be recorded on the Subject Adverse Event case report form and be followed to a satisfactory resolution.

In the unexpected event of an adverse event or a serious adverse event resulting from use of the investigational device, the Abbott monitor must be notified immediately by telephone and subsequently in writing within five (5) days of the occurrence. These adverse events must be described on the Device Adverse Event case report form. All adverse events are to be followed to satisfactory resolution, and any measures taken, as well as the follow-up, reported on the appropriate case report form.

IX. Statistical Procedures

A. General Information

All data analyses will be performed, and tables and listings of data will be provided by APOC using validated statistical software.

Additional subgroups of some testing sites and/or sample types may be created and analyzed.

If revised or additional analyses are required, a description of the additional or revised analyses and justifications for the changes will be documented and approved by the same functional areas as the original approvers to the protocol. This documentation will be included in the clinical study files.

The Abbott monitor will review all test results and may request that certain observations be deleted from analysis if there is an assignable cause, i.e., control or validity criteria failure, instrument errors or problems, acknowledged technologist error, and/or noncompliance with the study protocol. All results tested according to the protocol and not deleted will be eligible for analysis.

The statistical analysis output along with a listing containing each observation collected for this study will be completed. The listing will be printed for data

included in the analysis and excluded from the analysis. The excluded listing will include the reasons for exclusion.

It is expected that specimen collection will be completed at different times for each of the three assays (sodium, glucose and hematocrit) during the study. The data for a given assay may be analyzed against acceptance criteria once the specimen collection for that assay has been completed and may be used for different regulatory submissions (i.e. FDA response or 510(k) submission). Once specimen collection is determined to be completed, additional specimens will not be collected for that assay unless requested by a regulatory agency.

Interim data for a given assay (before specimen collection is completed) will not be evaluated against acceptance criteria. Interim data monitoring will be conducted to ensure the data meets validity criteria and minimum sample size requirements.

B. Statistical Analysis Description (Method Comparison)

1. Study Design

Method comparison testing will be performed using whole blood capillary specimens prospectively collected from routine patient care. This testing will be performed at a minimum of 3 sites. For each assay (glucose, hematocrit and sodium), testing of approximately 120 native and altered specimens will be performed in singlicate on both the i STAT 500 analyzer and the i STAT 1 Wireless analyzer. One (1) i-STAT 500 and one (1) i-STAT 1 Wireless analyzer will be used for this testing. Each site should collect and test approximately 100 specimens until sufficient specimens are collected and tested for study analysis. A minimum of one lot of i STAT EC4+ cartridges will be used for this testing.

2. Analysis Variables

The analysis variable for the method comparison study is the i-STAT EC4+ cartridge glucose concentration values (mg/dL), hematocrit values (%PCV and sodium concentration values (mmol/L).

3. Sample Size

The sample size is based on the recommendation of CLSI EP09-A3.
A minimum of 120 capillary whole blood specimens covering the measuring interval will be collected from a minimum of 3 sites. Each site should collect a minimum of 40 specimens.

Minimum of 3 sites
Within each site:
Number of lots = 1
i-STAT 1 Wireless analyzers = 1
i-STAT 500 analyzers = 1
Replicates per specimen = 1

4. Statistical Analysis Method

Perform the following analyses for glucose, hematocrit and sodium separately:

Analyses will be performed separately for each site and all sites combined.

Deming and Passing-Bablok linear regression analysis will be performed using the single replicate of the i-STAT 500 results versus the single replicate of the i-STAT 1 Wireless results. The slope, intercept, correlation coefficient and 95% confidence intervals for these values will be reported.

Scatter plots and Bland-Altman plots will be constructed as recommended in CLSI EP09-A3.

The predicted bias (difference) between the i-STAT 500 result and the i-STAT 1 Wireless result at the medical decision points and their 95% CIs will be calculated.

5. Level of Significance

Two-sided confidence intervals will be calculated at a 95% confidence level.

6. Data Handling Convention

All results from this testing that are performed according to the protocol and not excluded by the reviewers will be eligible for analysis. Reasons for any excluded results will be captured in the study database.

- Exclude the specimen from analysis if no results can be obtained from either the i-STAT 1 Wireless or the i-STAT 500.
- Exclude test results if there is an assignable cause.
- Exclude the specimen if the analyte value of interest (e.g., glucose, hematocrit or sodium) is outside of the measuring interval on either analyzer.

- Exclude a result obtained from a subject that is for a bucket of a given analyte that is already filled with the reason "Not part of analysis."

7. Outliers

The outlier criteria are based on CLSI document EP09-A3 Appendix B. The generalized Extreme Studentized Deviate (ESD) technique will be used to detect outliers.

X. Conduct of the Study

A. Responsibilities for Conduct of the Study

1) The investigator will have written and dated approval/favorable opinion from the Institutional Review Board (IRB) for the protocol and other documents as specified by the IRB before initiating the study. In some cases, the IRB may provide an expedited or exception review.
2) The investigator is responsible for reporting to the IRB and obtaining the necessary approvals from his/her site administration.
3) Abbott Laboratories will not initiate the study until the required pre-study documents are received from the site. Pre-study documents are aligned with GCP requirements and a detailed listing of the required pre-study documents will be provided to the investigator by the Abbott monitor.
4) The investigator will perform the study in accordance with GCP. The Abbott monitor will provide the investigator with the GCP-aligned list of investigator requirements.
5) The Abbott monitor will provide the investigator with the Guidance for Industry Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects (October 2009) for reference.
6) Abbott Laboratories has a responsibility under GCP to monitor this clinical study. The Abbott monitor will provide the investigator with the GCP-aligned list of responsibilities of the Abbott monitor.
7) The investigator will maintain a list of appropriately qualified persons to whom he/she has delegated significant study-related duties. This list must be updated as needed and the Abbott monitor must be notified of the changes.
8) The investigator will assure that all subjects are provided both written and oral informed consents, and that the subject's consent is documented in accordance

with local laws. In addition, every subject will be provided a copy of the consent form.

9) The investigator will maintain the subject's original consent form in the subject's permanent medical record or in the investigator's records, depending on site policy.

10) The investigator agrees to the requirement for guaranteed access to source data and to the investigator himself/herself by the IRB, Abbott monitor(s), auditors, and regulatory inspectors for the purpose of data verification or correction.

B. Withdrawal from Study

A subject's participation in this clinical study is voluntary and subject has the right to withdraw from the study any time without prejudice, however, the request to withdraw agreement does not include information that has already been made known or information gathered as a result of participation in the study.

If a subject fails to meet the inclusion/exclusion criteria or if the protocol required specimen is not obtained, the subject must be withdrawn from the study. All subjects enrolled in the study must be accounted for and the withdrawal of any subjects from the study will be documented on the appropriate CRF.

If another specimen can be redrawn that meets the specimen collection requirements, the specimen may be recollected from the subject. Alternatively, another subject may be enrolled into the study that meets the subject enrollment criteria.

All subjects enrolled in the study must be accounted for and the withdrawal of any subjects from the study will be documented on the appropriate CRF.

C. Protocol Amendments

All protocol amendments will be written and approved by Abbott Laboratories prior to its submission for IRB review and approval or exemption.

D. Protocol Deviations

A protocol deviation is defined as a planned or unplanned departure from the study protocol. All protocol deviations that occur during this study will be recorded on the protocol deviation CRF.

The investigator will not implement or deviate from the protocol without agreement from Abbott Laboratories and prior review and approval from the IRB. Exceptions to this include instances where it is necessary to eliminate an immediate hazard to

study subjects, or when the protocol changes involve only logistical or administrative aspects of the study.

Planned deviations from this protocol must be reported to the monitor prior to implementation. The implemented deviation and the circumstances regarding the deviation will be documented on the protocol deviation CRF. The monitor will approve in writing the inclusion of any specimen, which does not meet all of the inclusion or exclusion criteria of the study. The monitor may provide verbal approval prior to the written response.

E. Incident Reports

An incident CRF will be used to document any incident(s) that occur during the clinical study. An incident is defined as any unplanned or unexpected event that occurs with or without the input or intervention of the operator. The incident CRF should include a description of the incident, possible cause (if known), action taken, and identify any specimens that were affected.

F. Discontinuation of the Study

The study may be terminated prior to the stated time for reasons of safety or efficacy, or for other identified causes. The reason for discontinuation will be documented in the clinical study master file.

G. Site File/Record Storage

The investigator should arrange for the retention of all study documents in the site file. The investigator shall retain the site file records for at least a period of 2 years following the date a marketing application is approved; or if no application is to be filed or if the application is not approved for such an indication, until at least 2 years after the investigation is discontinued and the FDA is notified. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution when these documents no longer need to be retained.

H. Site Data

At the completion of the study a listing of the site's data generated during the study will be provided to each site.

I. Correspondence

All correspondence between the Abbott monitor and the testing site must be documented and retained as part of the study records (i.e. any telephone communication with the Abbott monitor should be documented in a telephone log; copies of e-mail messages should be printed).

XI. References

i-STAT 1 System Manual

CDRH guidance document. *Guidance on Informed Consent for in Vitro Diagnostic Analyzer Studies Using Leftover Human Specimens that are Not Individually Identifiable,* April 25, 2006.

Clinical and Laboratory Standards Institute (CLSI). Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition, CLSI document EP09-A3 (ISBN 1-56238-887-8 [Print]; ISBN 1-56238-888-6[Electronic]). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania, 19087, USA, 2013.

XII. Investigator's Agreement

By signing this statement the investigator agrees:

1. I have read and understand the contents of the clinical study protocol entitled Clinical Evaluation of i-STAT 500® Clinical Analyzer for Glucose, Hematocrit, and Sodium (Protocol No. CS-2016-0003 Version 6 dated October 04, 2016) and the i-STAT 500 Quick Reference Guide and will adhere to the study requirements as presented, and applicable local regulations.

2. I will protect the rights, safety, and well-being of subjects. Before initiating the study and where required by local regulations, an Institutional Review Board (IRB) will review and approve the study protocol and all other applicable study material. A copy of the approval of the study protocol will be submitted to Abbott Laboratories.

3. I will not use the results from products labeled as "For Investigational Use Only" for diagnostic purposes, because the performance characteristics of the product have not been established.

4. I understand that Abbott Laboratories, its designees, and regulatory authorities may require access to source documents for verification of study data.

5. I understand that if any questions arise, now or during the clinical evaluation, I will promptly contact the Abbott monitor or designee at Abbott Laboratories for clarification.

Investigator (Printed Name): _____

Investigator Title: _____

Investigator Signature: _____ Date: _____

Institution Name: _____

Institution Address: _____

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